Cleavage of the Wnt receptor Ryk regulates neuronal differentiation during cortical neurogenesis.

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Public Summary:

Scientific Abstract:
Ryk is a transmembrane receptor tyrosine kinase (RTK). It functions as a receptor of Wnt proteins required for cell-fate determination, axon guidance, and neurite outgrowth in different organisms; however, the molecular mechanism of Ryk signaling is unknown. Here, we show that Ryk is cleaved, permitting the intracellular C-terminal fragment of Ryk to translocate to the nucleus in response to Wnt3 stimulation. We also show that the cleaved intracellular domain of Ryk is required for Wnt3-induced neuronal differentiation in vitro and in vivo. These results demonstrate an unexpected mechanism of signal transduction for Ryk as a Wnt receptor, in which the intracellular domain itself functions as the transducing molecule to bring extracellular signals from the cell surface into the nucleus, to regulate neural progenitor cell differentiation.